

**SLIDES FOR OVERVIEW BY THOMAS LAUGHREN, M.D., FDA,
FOR PDAC MEETING ON FLUOXETINE FOR PMDD (11-3-99):**

**Fluoxetine in the Treatment of Premenstrual Dysphoric Disorder
(PMDD)**

- General questions regarding PMDD as a new indication**
- Specific questions regarding the NDA for fluoxetine in the treatment of PMDD**
- Questions requiring a vote**

PMDD as a New Indication

- Relevance of DSM-IV appendix status for PMDD?**
- PMDD as a distinct disorder, i.e., distinguishable from MDD?**
- Relationship of PMDD to PMS?**
- PMS as a candidate for an approved indication?**

Focus on Affective Symptoms in Fluoxetine/PMDD Program

- Appropriateness of VAS Mood-3 (for 19) and VAS Mood-4 (for 22) as primary outcomes?**
- General issue: total scale vs subscale**
- Implications for claim (affective symptoms of PMDD)?**

Continuous vs Luteal Phase Dosing for PMDD

- Fluoxetine program: continuous dosing**
- Published reports for other SSRIs: luteal phase dosing**
- Relevance of different possible dosing strategies to regulatory judgement for fluoxetine application?**

Exclusion of Oral Contraceptive (OC) Users

- Does PMDD occur in OC users?**
- Efficacy of fluoxetine as PMDD treatment in OC users?**
- Safety of fluoxetine in OC users?**

Relatively Small Fluoxetine Exposure in PMDD Program

- Substantial fluoxetine exposure in clinical trials of other disorders**
- Is this a reasonable extrapolation (for safety)?**

Crossover Design in Study 22

- Generally not a preferred design in psychiatric research**
- Argument: predictable cyclicity of PMDD favors crossover**
- Was the crossover design acceptable in study 22?**

Comment on Any Other PMDD Issues is Welcome

- Helpful to Division in:**
 - Reaching a judgement for fluoxetine application**
 - Advising other sponsors developing drugs for this population**
 - Reviewing future applications for PMDD and related indications**

Questions Requiring a Vote from the PDAC:

- 1. Has the sponsor provided evidence from more than one adequate and well controlled clinical investigation that supports the conclusion that Fluoxetine is effective for the treatment of Premenstrual Dysphoric Disorder (PMDD)?**
- 2. Has the sponsor provided evidence that Fluoxetine is safe when used in the treatment of PMDD?**

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